



PRESS RELEASE

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Lymphocytes that can reduce the size of tumours

Researchers from UNIGE have discovered the key role played by a receptor to trigger an immune response.

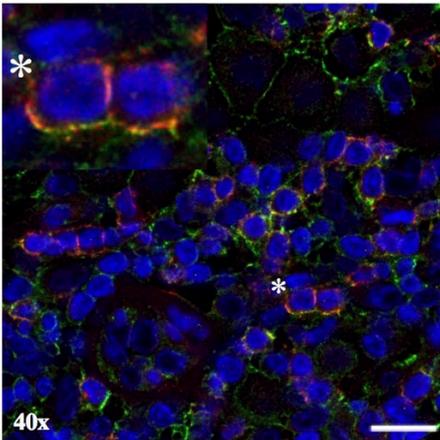
T-lymphocytes are key cells in the immune response. Their role is to identify infected or cancerous cells, recognised as being foreign to the body, for them to be destroyed. Understanding how they work and how to exploit them to fight cancer is therefore essential for devising new immunotherapies. By discovering on some T-lymphocytes a receptor that can be controlled by a tumour growth factor, researchers at the University of Geneva (UNIGE), Switzerland, have identified a cell population able to reduce the size of tumours. These results can be read in *EMBO Reports*.

Our cells have receptors — proteins — which, by binding to a factor specific to each receptor (known as a ligand) induce a cellular response. Although this activation is a crucial mechanism in cellular functioning, it can become pathogenic when it occurs haphazardly. C-met is one of these receptors: located mainly on epithelial cells, it is vital for embryonic development and tissue regeneration. Its ligand, HGF, is a cell growth factor that can become oncogenic if there is an abnormal c-Met activation, which is why HGF is detected so often in metastatic tumours.

The different types of lymphocytes serve as the backbone of the human immune system. They include CD8+ cytotoxic T-lymphocytes (“CD8 lymphocytes”), which are especially prominent in tumour-related inflammation. Professor Patrice Lalive, a neuro-immunologist in the Department of Pathology and Immunology at UNIGE Faculty of Medicine and a specialist of multiple sclerosis, recently discovered a disturbing fact when analysing these cells in detail: some CD8 lymphocytes carry the c-Met receptor. “Basically, our laboratory is studying the role of the HGF / c-Met pathway in autoimmune neurological diseases”, explains Prof. Lalive. “Discovering the c-Met receptor on CD8 lymphocytes was a surprise to us and pushed our research in the direction of cancer. It was not planned at all!”

A net effect on tumour size

The UNIGE scientists, supported by oncologist colleagues, investigated various animal models of cancer, as well as human tumour cells, to see whether the cells that express the receptor might have an effect. Results were very clear: in a pathological situation, the lymphocytes expressing the receptor succeeded in reducing the size of tumours. “By stimulating and then injecting these receptor-bearing lymphocytes into our diseased mice,” continues Prof. Lalive, “we managed



Detection of CD8+cMet+ lymphocytes in a tumour.

to cut the size of tumours. Conversely, if we inhibit the receptor, the tumour starts again with greater intensity.”

The research team then compared the anti-tumour action of CD8 lymphocytes carrying the c-Met receptor to those that do not. It turns out that lymphocytes that are equipped with the receptor are more effective. On the other hand, they are in a minority, even if they increase from about 5% of the CD8 lymphocytes present in blood to 10% in tumours. “In the immune-therapeutic arsenal that is currently available, there are already treatments based on blocking the activation of c-Met in tumour cells. But identifying c-Met on some CD8 lymphocytes means we can design new therapeutic pathways by stimulating CD8 lymphocytes equipped with c-Met receptors,” adds Professor Dietrich, a specialist in cancer immunotherapy at UNIGE and HUG, who took part in the work.

Results waiting confirmation

Prof. Lalive and his team have established a proof of principle by confirming, on the one hand, the anti-tumour action of this particular cell population in animal models of melanoma and, on the other, the presence of these lymphocytes in humans. “Now we have to demonstrate that this mechanism is found in other types of cancer and confirm its presence on human cells», says Prof. Lalive, before concluding: “We must also study the effects of the receptor on another type of lymphocyte, T CD4-lymphocytes, which plays an important role in autoimmune diseases such as multiple sclerosis. This shows that scientists have everything to gain by sometimes stepping outside their expert specialisation to gain a better understanding of living mechanisms.”

contact

Patrice Lalive

+41 22 372 83 18

Patrice.LaliveDepinay@unige.ch

UNIVERSITÉ DE GENÈVE
Communication Department

24 rue du Général-Dufour
CH-1211 Geneva 4

Tel. +41 22 379 77 17

media@unige.ch

www.unige.ch